REMARKS

Rejection under 35 U.S.C. § 103

Claim 7 remains rejected under § 103 over Maloney *et al.* (*Blood*, 1997) in view of Press *et al.* (*Lancet*, 1995), Kaminski *et al.* (*JCO*, 1996), Kaminski (U.S. Patent No. 6,287,537), and Wahl *et al.* (ASCO abstract, 1998).

For the convenience of the Office, the complete text of current claim 7 as presented in the amendment filed on 4 May 2006 is reproduced here:

> A method for treating a subject having CD20-positive B-cell lymphoma, wherein the subject is refractory to treatment with a non-radiolabeled rituximab antibody, comprising administering to the subject a therapeutically effective amount of an iodine-131-labeled murine anti-CD20 antibody.

The essential finding that supports the Office's position is that Kaminski '537 describes patients who are "refractory" to an unlabeled CD20 antibody because it teaches that certain patients respond to a combined regimen of unlabeled B1 antibody and radioimmunotherapy (RIT) with iodine-131-labeled B1 "only after an RIT dose."

Applicant reiterates the argument set forth at page 2, last full paragraph, of the reply filed on 9 October 2007, and the arguments stated in replies previous to that. However, applicant specifically withdraws the argument stated at the paragraph bridging pages 2-3 of the reply of 9 October 2007. In particular, the argument is inaccurate insofar as it asserts that the observation of "some antitumor effect" for a treatment in a patient is inconsistent with finding that the patient is "refractory" to the treatment. Clinical oncologists have come to use the term "refractory" to describe a relatively ineffective clinical response to treatment, typically characterized with respect to a shorter time to relapse (*e.g.*, an interval shorter than a specified minimum duration of response required to characterize at least a partial response) or a reduction in a measurable diagnostic criterion that is less than a certain percentage. The precise definition of "refractory" will depend on the criteria established to identify a clinical response to a particular agent. For example, for the purpose of a clinical trial discussed by Coleman *et al.* (*Blood*, 2003), of record, rituximab-refractory patients were defined as those who exhibited "no response or a duration of response of ≤6 months." To be sure, the art-recognized meaning of "refractory" includes a complete lack of response, but it is not limited only to that.

Even in view of this information, however, neither Kaminski reference provides evidence that supports a conclusion for obviousness as the Office suggests.

First, as argued in detail in the reply filed on 3 January 2007, the protocols reported in both the 1996 *JCO* article and the '537 patent were not designed to allow the experimenters to conclude whether or not any patients would have responded to a dose of unlabeled B1 antibody that would be expected to have therapeutic effect. In other words, there is insufficient information in the references to determine whether any patients in the trial could be categorized as "refractory" to a therapeutic dose of unlabeled B1.

Second, if Kaminski and coworkers had determined that some patients were refractory to unlabeled B1, then the express teachings of these references would not be logical. Specifically, Kaminski advocates – and the '537 patent claims – the use of an unlabeled CD20 antibody as a necessary step before the administration of an effective dose of radiolabeled CD20 antibody. *See* '537 claim 1, step (iii). If Kaminski considered that such a step had no effect, Kaminski would not have taught that it is advantageous to include it. The Office's finding is inconsistent with the teachings of the Kaminski references as a whole and cannot be relied upon to support its obviousness rationale. *See* M.P.E.P. § 2141.02, subsection VI.

Double patenting

Claim 7 was rejected under the nonstatutory doctrine of double patenting over certain claims of application serial no. 10/196,732. The '732 application is now abandoned, and accordingly this ground of rejection is moot.

Applicant notes that a continuing application claiming priority to the '732 application was filed on 18 August 2007. That application was assigned serial no. 11/840,956.

Conclusion

Applicant requests that the examiner reconsider the claim in light of the present remarks and withdraw the outstanding rejections.

Should the examiner have any concerns or questions, she is invited to contact the undersigned at the telephone number below.

Respectfully submitted,

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